Claims

What is claimed is:

1. A cyclic peptide having the formula:

(Z_1)-(X)-His-Ala-Val-(Y)-(Z_2)

wherein Z_1 and Z_2 are independently selected from the group consisting of amino acid residues and combinations thereof in which the residues are linked by peptide bonds; wherein Z_1 and Z_2 independently range in size from 1 to 10 residues; and wherein X and Y are independently selected from the group consisting of amino acid residues, wherein a disulfide bond is formed between residues X and Y.

2. A cyclic peptide according to claim 1, the peptide has an N-terminal acetyl, formyl or mesyl group.

3. A cyclic peptide according to claim 1, wherein X and Y are each independently selected from the group consisting of cysteine, penicillamine, β,β-tetramethylene cysteine, β,β-pentamethylene cysteine, β-mercaptopropionic acid, β,β-pentamethylene-β-mercaptopropionic acid, 2-mercaptobenzene, 2-mercaptoaniline and 2-mercaptoproline.

4. A cyclic peptide according to claim 1, wherein X and Y are cysteine residues.

5. A cyclic peptide according to claim 1, wherein the cyclic peptide comprises a sequence selected from the group consisting of: N-Ac-CHAVC-NH_2 (SEQ ID

NO:10), N-Ac-CHAVC-Y-NH_2 (SEQ ID NO:84), N-N-Ac-CHAVDC-NH_2 (SEQ ID NO:20), N-Ac-CHAVDIC-NH_2 (SEQ ID NO:50), N-Ac-CHAVDINC-NH_2 (SEQ ID NO:51), N-Ac-CHAVDINGC-NH_2 (SEQ ID NO:76), N-Ac-CAHAVC-NH_2 (SEQ ID NO:22), N-Ac-CAHAVDC-NH_2 (SEQ ID NO:26), N-Ac-CAHAVDIC-NH_2 (SEQ ID NO:24), N-Ac-CRAHAVDC-NH_2 (SEQ ID NO:28), N-Ac-CLRAHAVC-NH_2 (SEQ ID NO:30), N-Ac-CLRAHAVDC-NH_2 (SEQ ID NO:32), N-Ac-CSHAVC-NH_2 (SEQ ID NO:36), N-Ac-CFSHAVC-NH_2 (SEQ ID NO:85), N-Ac-CLFSHAVC-NH_2 (SEQ ID NO:_86), N-Ac-CHAVSC-NH_2 (SEQ ID NO:38), N-Ac-CSHAVSC-NH_2 (SEQ ID NO:40), N-Ac-CSHAVSSC-NH_2 (SEQ ID NO:42), N-Ac-CHAVSSC-NH_2 (SEQ ID NO:44), N-Ac-KHAVD-NH_2 (SEQ ID NO:12), N-Ac-DHAVK-NH_2 (SEQ ID NO:14), N-Ac-KHAVE-NH_2 (SEQ ID NO:16), N-Ac-AHAVDI-NH_2 (SEQ ID NO:34), N-Ac-SHAVDSS-NH_2 (SEQ ID NO:77), N-Ac-KSHAVSSD-NH_2 (SEQ ID NO:48), N-Ac-CHAVC-S-NH_2 (SEQ ID NO:87), N-Ac-S-CHAVC-NH_2 (SEQ ID NO:88), N-Ac-CHAVC-SS-NH_2 (SEQ ID NO:89), N-Ac-S-CHAVC-S-NH_2 (SEQ ID NO:90), N-Ac-CHAVC-T-NH_2 (SEQ ID NO:91), N-Ac-CHAVC-E-NH_2 (SEQ ID NO:92), N-Ac-CHAVC-D-NH_2 (SEQ ID NO:93), N-Ac-CHAVYC-NH_2 (SEQ ID NO:94), CH_3-SO_2-HN-CHAVC-Y-NH_2 (SEQ ID NO:95), CH_3-SO_2-HN-CHAVC-NH_2 (SEQ ID NO:96), HC(O)-NH-CHAVC-NH_2 (SEQ ID NO:96), N-Ac-CHAVPen-NH_2 (SEQ ID NO:97), N-Ac-PenHAVC-NH_2 (SEQ ID NO:98) and N-Ac-CHAVPC-NH_2. (SEQ ID NO:99),.

6. A cyclic peptide according to claim 5, wherein the cyclic peptide has an N-terminal acetyl group or CH_3-SO_2- group, and a C-terminal amide group.

7. A cyclic peptide comprising a dimer or multimer of the sequence His-Ala-Val.

8. A cell adhesion modulating agent comprising a cyclic peptide according to any one of claims 1-7.

9. A cell adhesion modulating agent according to claim 8 linked to a targeting agent.

10. A cell adhesion modulating agent according to claim 8 linked to a drug.

11. A cell adhesion modulating agent according to claim 8 linked to a solid support.

12. A cell adhesion modulating agent according to claim 11, wherein the solid support is a polymeric matrix.

13. A cell adhesion modulating agent according to claim 11, wherein the solid support is selected from the group consisting of plastic dishes, plastic tubes, sutures, membranes, ultra thin films, bioreactors and microparticles.

14. A cell adhesion modulating agent according to claim 13, further comprising one or more of:

(a) a cell adhesion recognition sequence that is bound by an adhesion molecule other than a cadherin, wherein the cell adhesion recognition sequence is separated from any HAV sequence(s) by a linker; and/or

(b) an antibody or antigen-binding fragment thereof that specifically binds to a cell adhesion recognition sequence bound by an adhesion molecule other than a cadherin.

15. A cell adhesion modulating agent according to claim 14, wherein the adhesion molecule is selected from the group consisting of integrins, occludin, N-CAM, desmogleins, desmocollins, fibronectin, laminin and other extracellular matrix proteins.

16. A cell adhesion modulating agent according to claim 8 linked to a detectable marker.

17. A pharmaceutical composition comprising a cell adhesion modulating agent according to claim 8, in combination with a pharmaceutically acceptable carrier.

18. A composition according to claim 17, further comprising a drug.

19. A composition according to claim 17, wherein the cell adhesion modulating agent is present within a sustained-release formulation.

20. A pharmaceutical composition according to claim 17, further comprising one or more of:

(a) a peptide comprising a cell adhesion recognition sequence that is bound by an adhesion molecule other than a cadherin; and/or

(b) an antibody or antigen-binding fragment thereof that specifically binds to a cell adhesion recognition sequence bound by an adhesion molecule other than a cadherin.

21. A pharmaceutical composition according to claim 20, wherein the adhesion molecule is selected from the group consisting of integrins, occludin, N-CAM, desmogleins, desmocollins, fibronectin, laminin and other extracellular matrix proteins.

22. A method for reducing the size of a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent according to claim 8, and thereby reducing the size of the tumor.

23. A method for modulating apoptosis in a cadherin-expressing cell, comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby modulating apoptosis.

24. A method for enhancing cadherin-mediated cell adhesion comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby enhancing cell adhesion.

25. A method for modulating angiogenesis comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby modulating angiogenesis.

26. A method for modulating endothelial cell adhesion, comprising contacting a cadherin expressing cell with a modulating agent according to claim 8, and thereby modulating endothelial cell adhesion.

27. A method for stimulating blood vessel regression, comprising contacting a blood vessel with a cell adhesion modulating agent according to claim 8, and thereby stimulating blood vessel regression.

28. A method for increasing vasopermeability in a mammal, comprising contacting a cadherin-expressing endothelial cell with a cell adhesion modulating agent according to claim 8, and thereby increasing vasopermeability.

29. A method for facilitating wound healing, comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby facilitating wound healing.

30. A method for disrupting neovasculature in a mammal, comprising contacting a cadherin expressing cell with a cell adhesion modulating agent according to claim 8, and thereby disrupting neovasculature.

31. A method for enhancing the survival of neurons comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby enhancing the survival of neurons.

32. A method for suppressing neural injury comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby suppressing neural injury.

33. A method for modulating neurite outgrowth comprising contacting a cadherin expressing neural cell with a cell adhesion modulating agent according to claim 8,

and thereby modulating neurite outgrowth.

34. A method for modulating vascular smooth muscle cell migration, comprising contacting a vascular smooth muscle cell with a cell adhesion modulating agent according to claim 8, and thereby modulating vascular smooth muscle cell migration.

35. A method for modulating vascular smooth muscle cell apoptosis, comprising contacting a vascular smooth muscle cell with a cell adhesion modulating agent according to claim 8, and thereby modulating vascular smooth muscle cell apoptosis.

36. A method for preventing the formation or advance of restenosis, comprising contacting a cadherin expressing cell with a cell adhesion modulating agent according to claim 8, and thereby preventing the formation or advance of restenosis.

37. A method for maintaining vessel luminal area following vascular trauma, comprising contacting a cadherin expressing cell with a cell adhesion modulating agent according to claim 8, and thereby maintaining vessel luminal area following vascular trauma.

38. A method for treating a traumatized vessel, comprising contacting a cadherin expressing cell with a cell adhesion modulating agent according to claim 8, and thereby treating a traumatized vessel.

39. A method for enhancing drug delivery to the central nervous system of a mammal comprising administering to a mammal a cell adhesion modulating agent according to claim 8, and thereby enhancing drug delivery to the central nervous system.

40. A method for enhancing adhesion of foreign tissue implanted within a mammal, comprising contacting a site of implantation of foreign tissue in a mammal with a cell adhesion modulating agent according to claim 8, and thereby enhancing adhesion of the foreign tissue.

41. A method for treating a demyelinating neurological disease in a mammal, comprising administering to a mammal a cell adhesion modulating agent according to claim 8, and thereby treating the demyelinating neurological disease.

42. A method for facilitating migration of a cadherin expressing cell on astrocytes, comprising contacting a cadherin expressing cell with (a) a cell adhesion modulating agent that inhibits cadherin-mediated cell adhesion, wherein the modulating agent according to claim 8; and (b) one or more astrocytes; and thereby facilitating migration of the cadherin expressing cell on the astrocytes.

43. A method for modulating the immune system of a mammal, comprising administering to a mammal a cell adhesion modulating agent according to claim 8, wherein the modulating agent inhibits cadherin-mediated cell adhesion, and thereby modulating the immune system of a mammal.

44. A method for preventing pregnancy in a mammal, comprising administering to a mammal a cell adhesion modulating agent according to claim 8, wherein the modulating agent inhibits cadherin-mediated cell adhesion, and thereby preventing pregnancy in a mammal.

45. A method for increasing vasopermeability in a mammal, comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby increasing vasopermeability.

46. A method for inhibiting synaptic stability in a mammal, comprising contacting a cadherin-expressing cell with a cell adhesion modulating agent according to claim 8, and thereby inhibiting synaptic stability in a mammal.

47. A method for facilitating the removal of hair follicles from skin, comprising contacting a cadherin expressing cell with a modulating agent according to claim

8, and thereby facilitating the removal of hair follicles from the skin.

48. A method for increasing blood flow to a tumor, comprising contacting a tumor with a modulating agent according to claim 8, and thereby increasing blood flow to a tumor.

49. A method for inhibiting the development of endometriosis in a mammal, comprising contacting a cadherin expressing cell with a modulating agent according to claim 8, and thereby inhibiting the development of endometriosis.

50. A method for modulating adipogenesis comprising contacting a cadherin-expressing cell with a modulating agent according to claim 8, and thereby modulating adipogenesis.

51. A method for modulating a tumor permeability barrier to drugs, comprising contacting a cadherin-expressing cell with a modulating agent according to claim 8, and thereby modulating a tumor permeability barrier.

52. A method for the modulation of bone adhesion, comprising contacting a cadherin-expressing cell with a modulating agent according to claim 8, and thereby modulating bone adhesion.

53. An implantable medical device or material linked to, coated with or having interspersed within, a cell adhesion modulating agent according to claim 8.

54. The medical device of claim 53, wherein the medical device is selected from the group consisting of a balloon, stent, shunt, catheter, stent graft, vascular graft, vascular patch, filter, adventitial wrap, intraluminal paving system, cerebral stent, cerebral aneurysm filter coil, myocardical plug, pacemaker lead, dialysis access graft, and heart valve.